DRAFT REVISED MONOGRAPH FOR COMMENTS

This draft revised monograph contain text for inclusion in the Indian Pharmacopoeia (IP). The content of this draft document is not final, and the text may be subject to further revisions prior to publication in the IP. This draft does not necessarily represent the decisions or the stated policy of the IP or Indian Pharmacopoeia Commission (IPC).

Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Comments received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in/ biologics-ipc@gov.in **before the last date for comments.**

Document History and Schedule for the Adoption Process

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Bluetongue Vaccine, Inactivated

Bluetongue Vaccine (BTV), Inactivated is a preparation containing bluetongue virus serotypes that have been inactivated in such a manner that is immunogenic activity is retained. This monograph applies to vaccines intended for the active immunization of sheep against bluetongue. The vaccine can also be used in other susceptible animals such as goats, cattle and wild animals.

Production

Preparation of the Vaccine

Each serotype of bluetongue virus is grown separately in suitable cell culture. Each virus serotype should have a $TCID_{50}$ of $10^{5.5}$ per ml. The harvested virus is inactivated by using Binary Ethyleneimine Formaldehyde or Ethyleneimine in suitable condition. The inactivated blue tongue virus serotypes are blended. The vaccine contains a suitable adjuvant.

Substrate for virus propagation

Cell cultures. If the vaccine virus is grown in cell cultures, they comply with the requirements for cell cultures for production of veterinary vaccines (2.7.13). If continuous cell line is used for the vaccine manufacturing, the cell line should be from seed lot system.

Master seed lot

Identification. When injected into susceptible sheep, the vaccine stimulates the production of specific neutralizing antibodies against the BTV serotypes.

Extraneous agents (2.7.19). The master seed lot complies with the test for extraneous agents.

Inactivation

Carry out inactivation of BTV serotypes separately. During inactivation of the virus, take the sample at regular intervals for the purpose of monitoring the rate and linearity of inactivation process. Virus titres in the samples are determined by inoculation into sensitive cell culture. The infectivity of the timed samples is plotted against time. The last sample taken does not show cytopathic effect or the presence of BTV in the inoculated sensitive cell culture. The inactivation procedure is considered satisfactory if the inoculated sensitive cell culture does not show the presence of BTV.

Choice of vaccine composition. A reference strain obtained from an authentic source shall be used for the vaccine production. The master seed which has been established as pure, safe and immunogenic shall be used for vaccine production. The vaccine is shown to be satisfactory with respect to safety (2.7.7) and efficacy (2.7.12). The following tests for safety and immunogenicity may be used during the demonstration of safety and efficacy.

Safety

Carry out the test for each route and method of administration to be recommended for the vaccination. Representative batches prepared from the master seed shall be injected per batch into each of six sheep with double doses of the vaccine and by the route stated on the label. Observe the sheep for 14 days. None of the sheep shows abnormal local or systemic reactions. Such animals used in the test may be free of bluetongue antibodies for the serotypes present in the vaccine.

Immunogenicity

Inject each of ten susceptible sheep that have been previously tested and shown to be free from bluetongue antibodies for the serotypes present in the vaccine with the minimum dose and the route stated on the label. After 14 days, administer a booster dose. 14 days later, collect the serum from each sheep and carry out serum neutralization test in suitable cell cultures using 100 $TCID_{50}$ of each of the BTV serotypes separately. Include three sheep's as unvaccinated controls. The vaccine passes the test if mean antibody titre of the vaccinated group is more than 1:20. The test is valid only if no specific antibodies are found in the control sheep.

Manufacturer's tests

Identification. The vaccine complies with the requirements of test mentioned under section of master seed lot. Alternatively suitable validated immunochemical/ molecular biology methods can be used with the approval of competent authority

Residual live virus. The vaccine complies with the inactivation test mentioned under master seed lot.

Potency

The vaccine complies with the requirements of the test prescribed under Immunogenicity when administered according to the recommended schedule by a recommended route and method.

Batch tests

Identification

The vaccine complies with the requirements of test mentioned under section of master seed lot. Potency test serves the purpose of identification also.

Sterility (2.2.11). Complies with the test for sterility.

Potency

The vaccine complies with the requirements of the test prescribed under Immunogenicity when administered according to the recommended schedule by a recommended route and method.

Safety

Use two susceptible sheep, which have never been vaccinated against bluetongue and are free from neutralizing antibodies to bluetongue virus serotypes used in the vaccine. Inoculate each of two sheep with double dose of the test vaccine by route stated on the label. Observe the animals for 14 days. The vaccine complies with the test if no animal shows abnormal local or systemic reactions attributable to the vaccine during the observation period.

Note: General Requirements shall be referred regarding omission of the batch safety test.

Labelling.

The label must state that (1) BTV serotypes used; (2) recommended age for vaccination the vaccine is for veterinary use only; (3) the recommended routes of administration; (4) the instructions for use, such as shake well before use (5) the animal species for which the vaccine is intended; (6) storage temperatures; (7) Batch Number, Manufacturing date and expiry date; (8) Total volume or number of doses; (9) Dose of vaccine